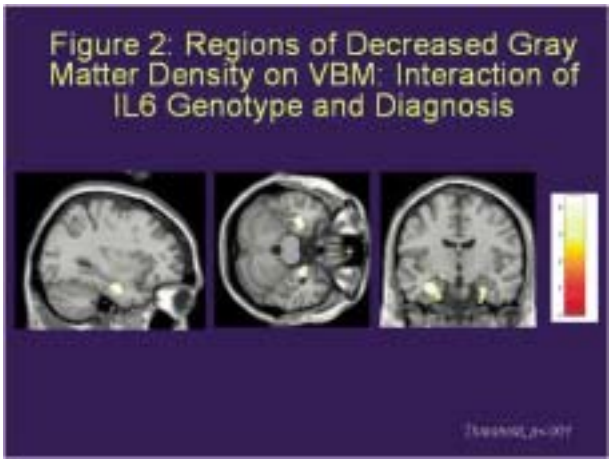

O1-03-02 REGIONAL DECLINE OF BRAIN PERFUSION IN HEALTHY AGING DETECTED WITH ARTERIAL SPIN LABELING AT 4T

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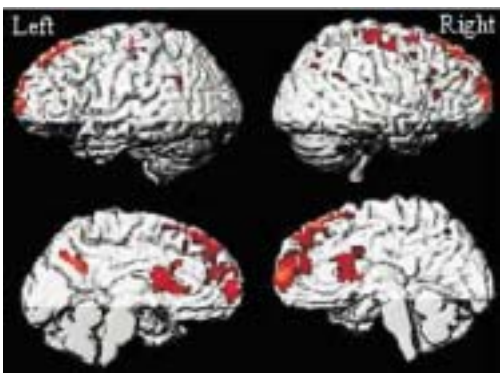
Background: While anatomical MRI studies of aging report brain atrophy, an age-related decline of brain perfusion remains controversial. **Objective:** Utilizing the increased sensitivity of arterial spin labeling (ASL) at higher magnetic fields, we conducted a pilot study at 4 Tesla on 12 healthy volunteers (age 22 -77 years) to explore if ASL-MRI detects age-related hypoperfusion. **Methods:** A pulsed ASL version was used to acquire multislice perfusion weighted MRI data of the brain at 2.4 x 2.4 x 5mm spatial resolution. To account for brain atrophy, perfusion images were registered to structural images, corrected for partial volume effects and spatially normalized to a study-specific brain template for voxel-wise statistical analysis. Regions of significant correlations between hypoperfusion and age are superimposed on a surface rendered brain template (see figure). The most prominent correlations between hypoperfusion and age occured in the right superior and frontal gyrus (both $p<0.001$), the caudate nucleus ($p<0.001$), bilaterally in the anterior cingulate ($p<0.01$), and in the precentral gyrus ($p<0.05$), while most posterior brain regions were spared. Referencing the perfusion data to perfusion of motor cortex in each subject to eliminate global variations of perfusion did not substantially alter the pattern. **Conclusions:** This pattern sharply contrasts with the prominent patterns seen in subjects with mild cognitive impairment or Alzheimer's disease that involve parietal lobe, including the posterior cingulate. This would suggest that cognitive decline in healthy aging is a different entity than the progressive cognitive decline seen in mild cognitive impairments and Alzheimer's disease. If these patterns were confirmed, this would establish a key role for ASL-MRI in differentiating between changes in brain function, which might indicate incipient dementia and those related to normal aging. However, these results need to be confirmed on a larger number of subjects and perfusion needs to be quantified.



O1-03-03 PREDICTING MCI PROGRESSION TO AD VIA AUTOMATED ANALYSIS OF T1-WEIGHTED MR IMAGE INTENSITY

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Background: Amnestic Mild Cognitive Impairment (MCI) individuals are known to be at risk for progression to AD. There is evidence that in those who will progress, measurable hippocampal and entorhinal cortex atrophy, demonstrable on T1-weighted (T1w) MR serves as a moderate, though labor-intensive, predictor. **Objective:** We aimed at predicting progression to AD from MCI using a recently developed automated classification technique that compares T1w MRI intensity of patients to database normal controls. This technique utilizes the full extent of volume differences in the medial temporal lobe (MTL), rather than being limited to single structures. **Methods:** Subjects - 16 amnestic MCI [age 77.7(5.1) yrs, MMSE 26.9 (2.4) at baseline scan] that subsequently progressed to AD in 2.6 (1.6) yrs, and 8 non-progressing amnestic MCI [age 80.3 (6.3) yrs, MMSE 28.5 (1.2) at baseline scan, follow-up 5.7 (4.0) yrs]. T1w MRI were acquired after informed consent on a 1.5T GE Signa 5 scanner (3D sequence, TR= 300ms, TE= 4.2ms, FA = 90, sagittal acquisition with 256 (SI) x 256 (AP) 0.86 mm pixels, 5 mm slices). Pre-processing - All scans were corrected for intensity inhomogeneity, linearly registered (9 DoF) in stereotaxic space, resampled to a $1mm^3$ grid and intensity normalized. Rectangular volumes of interest (VOI) were defined on the left and right MTL (80x52x60 voxels). Each VOI was further linearly registered (12 DoF) to a reference target image. Analysis - Normative intensity spaces were created using principal components analysis of VOIs for a training set composed of 152 normal young subjects. Intensity from the pre-processed scans from the study subjects were projected in the normative spaces. Leave-one-out, forward stepwise linear discriminant analyses (P-to-enter < 0.01) retained 2 projection eigenvectors for classification. Sensitivity to progression to AD was 94% (15/16), specificity 75% (6/8) and accuracy 88% (21/24). **Conclusion:** Our results indicate that MR data projected in multidimensional feature domains has the potential to adequately predict progression of amnestic MCI to AD, on average 2.6 yrs before a clinical diagnostic. This single-scan, practical, automatic, and objective method therefore holds promise for early AD detection.

O1-03-04 RADIOIODINATED HYDROXY QUINOLINE DERIVATIVES AS PROBES FOR AMYLOID PLAQUE IMAGING AND ENHANCED BRAIN DELIVERY VIA NANOPARTICLES IN MICE

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Objectives: Metal ion binding sites on amyloid beta (abeta) aggregates provide a promising target for the development of novel diagnostic and therapeutic agents. We had reported radiolabeling of radioiodinated Clioquinol (CQ) and oxine (HQ). Here we report evaluation of their application as amyloid plaque imaging agents and nanoparticle-mediated delivery of the tracers to the brain. **Methods:** Biodistribution of radioiodinated (^{125}I) CQ, HQ and butyl cyanoacrylate nanoparticles loaded with ^{125}I CQ was